CIP A 17

UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/417,268	10/13/99	CHENCHIK	A CLON-008

HM12/0727

BRET FIELD
BOZICEVIC FIELD & FRANCIS LLP
200 MIDDLEFIELD ROAD
SUITE 200
MENLO PARK CA 94025

EXAMINER	
FORMAN, B	
ART UNIT	**PAPER NUMBER**
1655	21

DATE MAILED: 07/27/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/417,268	Applicant(s) CHENCHIK, ALEX	
	Examiner BJ Forman	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,53 and 57-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,53 and 57-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to papers filed 23 May 2001 in Paper No. 20 in which claims 1, 57, 58 and 60 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejection in the Office Action of Paper No. 19 dated 5 April 2001 under 35 U.S.C. 112, second paragraph are maintained. The previous rejections under 35 U.S.C. 102(e) and 35 U.S.C. 103(a) are withdrawn in view of the amendments. All of the arguments have been thoroughly reviewed but are deemed moot in view of the amendments and new grounds for rejection. New grounds for rejection are discussed.

Currently claims 1-17, 53 and 57-77 are under prosecution.

Claim Rejections - 35 USC § 112

2. Claims 1-17, 53 & 60-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 1-17, 53 & 60-77 are indefinite in Claims 1 & 60 for the recitation "stably associated with" because "stably" is a relative term that requires definition or criteria for determining and because "associated with" is a non-specific relational phrase and therefore the relationship between the "spots" and the "support" is not defined. It is suggested that Claims 1 & 60 be amended to define or recite criteria for determining "stably" and to define the relationship between the "spots" and "support" e.g. replace "stably associated with" with "attached to".

Response to Arguments

4. Applicant argues that "stably associated" when read in light of the specification by one of skill in the art is not indefinite. This argument is not found persuasive because "stably" is a relative term but it is unclear in what relationship the "association" is "stable" i.e. the

"association" is "stable" relative to covalent bonds; relative to non-covalent bonds; or relative to hydrogen bonds. Additionally, the conditions under which the "association is "stable" is undefiined i.e. is the "association" "stable" during hybridization; during denaturation; during washing in water; during washing in high salt solution and/or low salt solution; during high temperature washing etc. While the claims are read in light of the specification, limitations from the specification cannot be read into the claims. It is suggested that the claim be amended to define "stably associated".

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3, 5, 10, 12, 13, 57, 60-62, 64, 69, 71 and 72 are rejected under 35 U.S.C. 102(b) as being anticipated Letsinger et al. (U.S. Patent No. 5,681,943, issued 28 October 1997).

Regarding Claim 1, Letsinger et al. disclose an array comprising at least on pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides (Column 7, line 65-Column 8, line 21).

Regarding Claim 2, Letsinger et al. disclose the array wherein said plurality of unique oligonucleotides hybridize to different regions of said target nucleic acid (Column 8, lines 10-12).

Regarding Claim 3, Letsinger et al. disclose the array wherein said plurality of unique oligonucleotides hybridize to non-overlapping regions of said target nucleic acid i.e. they bind at adjacent positions on the target (Column 5, lines 31-34).

Regarding Claim 5, Letsinger et al. disclose the array wherein two or more different target nucleic acids are represented in said pattern i.e. multiple point mutations (Column 7, lines 65-67).

Regarding Claim 10, Letsinger et al. disclose the array wherein each of said oligonucleotides ranges from 15 to about 150 nucleotides in length (Column 5, lines 31-38).

Regarding Claim 12, Letsinger et al. disclose the array wherein said plurality ranges from about 3 to 50 oligonucleotides in number (Column 8, lines 22-25).

Regarding Claim 13, Letsinger et al. disclose the array wherein said oligonucleotide spots correspond to the same type of target nucleic acid i.e. point mutation-specific (Column 7, lines 65-67).

Regarding Claim 57, Letsinger et al. disclose an array comprising a pattern of oligonucleotide spots, wherein each probe oligonucleotide spot comprises an oligonucleotide probe composition consisting of a mixture of 3 to 50 unique oligonucleotides of different sequence (Column 8, lines 22-27) and from about 15 to 150 nucleotides in length (Column 5, lines 31-38) that hybridize to a different region of the same target nucleic acid to produce a complex made up of said target nucleic acid and two or more unique oligonucleotides (Column 7, line 65-Column 8, line 21).

Regarding Claim 60, Letsinger et al. disclose an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that cooperatively hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides (Column 7, line 65-Column 8, line 21).

Regarding Claim 61, Letsinger et al. disclose the array wherein said plurality of unique oligonucleotides hybridize to different regions of said target nucleic acid (Column 8, lines 10-12).

Regarding Claim 62, Letsinger et al. disclose the array wherein said plurality of unique oligonucleotides hybridize to non-overlapping regions of said target nucleic acid i.e. they bind at adjacent positions on the target (Column 5, lines 31-34).

Regarding Claim 64, Letsinger et al. disclose the array wherein two or more different target nucleic acids are represented in said pattern i.e. multiple point mutations (Column 7, lines 65-67).

Regarding Claim 69, Letsinger et al. disclose the array wherein each of said oligonucleotides ranges from 15 to about 150 nucleotides in length (Column 5, lines 31-38).

Regarding Claim 71, Letsinger et al. disclose the array wherein said plurality ranges from about 3 to 50 oligonucleotides in number (Column 8, lines 22-25).

Regarding Claim 72, Letsinger et al. disclose the array wherein said oligonucleotide spots correspond to the same type of target nucleic acid i.e. point mutation-specific (Column 7, lines 65-67).

7. Claims 4-9, 14-17, 58, 63, 65-68 and 73-76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Letsinger et al. (U.S. Patent No. 5,681,943, issued 28 October 1997) in view of Pinkel et al. (U.S. Patent No. 5,830,645, filed 9 December 1994).

Regarding Claim 4, Letsinger et al. teach an array comprising at least on pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides (Column 7, line 65-Column 8, line

21) but they do not teach said plurality of unique oligonucleotides hybridized to overlapping regions of said target nucleic acid. Pinkel et al. teach a similar array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid (Example 1, Column 13-14). While they do not teach the fragments hybridized to overlapping regions of said target, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the complete digestion of Pinkel et al. with a partial digestion to thereby provide fragments which hybridize to overlapping regions for the obvious benefit of optimizing hybridization and signal production for a given hybridization procedure e.g. mapping the target as taught by Pinkel et al. (Column 4, lines 34-44). Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the non-overlapping probes of Letsinger et al. to provide overlapping probes the obvious benefit of optimizing hybridization and signal production for a given hybridization procedure e.g. mapping the target as taught by Pinkel et al. (Column 4, lines 34-44).

Regarding Claim 5, Letsinger et al. teach the array wherein two or more different target nucleic acids are represented in said pattern i.e. multiple point mutations (Column 7, lines 65-67) and Pinkel et al. teach the similar array wherein two different target nucleic acids are represented in said pattern i.e. cMYC and 21D7 (Column 13, lines 10-18).

Regarding Claim 6, Letsinger et al. teach the array wherein multiple mutations are analyzed simultaneously (Column 7, lines 65-67) but they do not teach each probe spot corresponds to a different target nucleic acid. However, Pinkel et al. teach the similar array wherein each oligonucleotide spot corresponds to a different target nucleic acid i.e. anonymous clones (Column 4, lines 19-23). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the multiple-mutation array of Letsinger et

al. to provide mutation-specific spots i.e. target-specific spots as taught by Pinkel et al. for the obvious benefit simplicity i.e. identifying mutation by location-specific hybrid detection as taught by Pinkel et al. (Column 4, lines 6-24).

Regarding Claim 7, Letsinger et al. teach the array wherein multiple mutations are analyzed simultaneously (Column 7, lines 65-67) but they do not teach two or more spots corresponds to the same target. However, Pinkel et al. teach the similar array wherein two or more oligonucleotide spots correspond to the same target nucleic acid i.e. cMYC and 21D7 (Column 13, lines 10-18 and Fig. 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the analytical array of Letsinger et al. to provide comparative hybridization signals as taught by Pinkel et al. (Fig. 1) for the obvious benefit of comparing sample hybridization to reference hybridization to thereby accurately diagnose the presence or absence of a mutation by simply comparing a signal.

Regarding Claim 8, Letsinger et al. said array comprises a plurality of mutation-specific probes (Column 7, lines 65-67) but they do not teach said array comprises a plurality of patterns. However, Pinkel et al. teach the similar array wherein said array comprises a plurality of said patterns of oligonucleotide spots (Fig.1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Letsinger et al. to provide said probe spots in a plurality of patterns as illustrated by Pinkel et al. wherein each pattern comprises known sequences at known locations within the pattern for the expected benefit of simply identifying probe-target complexes based on complex location within the pattern.

Regarding Claim 9, Pinkel et al. teach the spots are arrayed for individual detection by optimizing spot size and substrate material etc. (Column 8, lines 31-40) but they do not teach said plurality of patterns are separated from each other by walls. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrayed spots of Pinkel et al. by separating the spots from each other by walls for the

obvious benefit of physically separating the spots by walls to thereby facilitate individual detection.

Regarding Claim 14, Letsinger et al. does not teach the density of spots. Pinkel et al. teach the array wherein the density of spots does not exceed about 1000/cm^2 (Column 4, lines 6-29).

Regarding Claim 15, Letsinger et al. does not teach the density of spots. Pinkel et al. teach the array wherein the density of spots does not exceed about 400/cm^2 (Column 4, lines 6-29).

Regarding Claim 16, Letsinger et al. does not teach the number of spots. Pinkel et al. teach the array wherein the number of spots on said array ranges from about 50 to 10,000 i.e. 96 (Column 4, lines 24-29).

Regarding Claim 17, Letsinger et al. does not teach the number of spots. Pinkel et al. teach the array wherein the number of spots on said array ranges from about 50 to 1,000 i.e. 96 (Column 4, lines 24-29).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the number and density of probes spots on the array wherein the number and density of probes is selected based on target and assay for which the array will be used as taught by Pinkel et al. (Column 4, lines 6-33) to the array of Letsinger et al. for the obvious benefits of providing a target and assay specific array to thereby optimize assay conditions and maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 58, Letsinger et al. teach an array comprising a pattern of oligonucleotide spots, wherein each probe oligonucleotide spot comprises an oligonucleotide probe composition consisting of a mixture of 3 to 50 unique oligonucleotides of different sequence (Column 8, lines 22-27) and from about 15 to 150 nucleotides in length (Column 5,

lines 31-38) that hybridize to a different region of the same target nucleic acid to produce a complex made up of said target nucleic acid and two or more unique oligonucleotides (Column 7, line 65-Column 8, line 21) but they do not teach the array comprises a pattern of oligonucleotide spots that does not exceed about 400 spots/cm^2. However, Pinkel et al. teach the array wherein the density of spots does not exceed about 400/cm^2 (Column 4, lines 6-29). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the number and density of probes spots on the array wherein the number and density of probes is selected based on target and assay for which the array will be used as taught by Pinkel et al. (Column 4, lines 6-33) to the array of Letsinger et al. for the obvious benefits of providing a target and assay specific array to thereby optimize assay conditions and maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

Regarding Claim 63, Letsinger et al. disclose an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that cooperatively hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides (Column 7, line 65-Column 8, line 21) but they do not teach said plurality of unique oligonucleotides hybridized to overlapping regions of said target nucleic acid. Pinkel et al. teach a similar array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid (Example 1, Column 13-14). While they do not teach the fragments hybridized to overlapping regions of said target, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the

complete digestion of Pinkel et al. with a partial digestion to thereby provide fragments which hybridize to overlapping regions for the obvious benefit of optimizing hybridization and signal production for a given hybridization procedure e.g. mapping the target as taught by Pinkel et al. (Column 4, lines 34-44). Additionally, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the non-overlapping probes of Letsinger et al. to provide overlapping probes the obvious benefit of optimizing hybridization and signal production for a given hybridization procedure e.g. mapping the target as taught by Pinkel et al. (Column 4, lines 34-44).

Regarding Claim 64, Letsinger et al. teach the array wherein two or more different target nucleic acids are represented in said pattern i.e. multiple point mutations (Column 7, lines 65-67) and Pinkel et al. teach the similar array wherein two different target nucleic acids are represented in said pattern i.e. cMYC and 21D7 (Column 13, lines 10-18).

Regarding Claim 65, Letsinger et al. teach the array wherein multiple mutations are analyzed simultaneously (Column 7, lines 65-67) but they do not teach each probe spot corresponds to a different target nucleic acid. However, Pinkel et al. teach the similar array wherein each oligonucleotide spot corresponds to a different target nucleic acid i.e. anonymous clones (Column 4, lines 19-23). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the multiple-mutation array of Letsinger et al. to provide mutation-specific spots i.e. target-specific spots as taught by Pinkel et al. for the obvious benefit simplicity i.e. identifying mutation by location-specific hybrid detection as taught by Pinkel et al. (Column 4, lines 6-24).

Regarding Claim 66, Letsinger et al. teach the array wherein multiple mutations are analyzed simultaneously (Column 7, lines 65-67) but they do not teach two or more spots corresponds to the same target. However, Pinkel et al. teach the similar array wherein two or more oligonucleotide spots correspond to the same target nucleic acid i.e. cMYC and 21D7 (Column 13, lines 10-18 and Fig. 1). It would have been obvious to one of ordinary skill in the

art at the time the claimed invention was made to modify the analytical array of Letsinger et al. to provide comparative hybridization signals as taught by Pinkel et al. (Fig. 1) for the obvious benefit of comparing sample hybridization to reference hybridization to thereby accurately diagnose the presence or absence of a mutation by simply comparing a signal.

Regarding Claim 67, Letsinger et al. said array comprises a plurality of mutation-specific probes (Column 7, lines 65-67) but they do not teach said array comprises a plurality of patterns. However, Pinkel et al. teach the similar array wherein said array comprises a plurality of said patterns of oligonucleotide spots (Fig. 1). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Letsinger et al. to provide said probe spots in a plurality of patterns as illustrated by Pinkel et al. wherein each pattern comprises known sequences at known locations within the pattern for the expected benefit of simply identifying probe-target complexes based on complex location within the pattern.

Regarding Claim 68, Pinkel et al. teach the spots are arrayed for individual detection by optimizing spot size and substrate material etc. (Column 8, lines 31-40) but they do not teach said plurality of patterns are separated from each other by walls. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrayed spots of Pinkel et al. by separating the spots from each other by walls for the obvious benefit of physically separating the spots by walls to thereby facilitate individual detection.

Regarding Claim 73, Letsinger et al. does not teach a density of probe spots. Pinkel et al. disclose the array wherein the density of spots does not exceed about 1000/cm^2 (Column 4, lines 6-29).

Regarding Claim 74, Letsinger et al. does not teach a density of probe spots. Pinkel et al. disclose the array wherein the density of spots does not exceed about 400/cm^2 (Column 4, lines 6-29).

Regarding Claim 75, Letsinger et al. does not teach a number of probe spots. Pinkel et al. disclose the array wherein the number of spots on said array ranges from about 50 to 10,000 i.e. 96 (Column 4, lines 24-29).

Regarding Claim 76, Letsinger et al. does not teach a number of probe spots. Pinkel et al. disclose the array wherein the number of spots on said array ranges from about 50 to 1,000 i.e. 96 (Column 4, lines 24-29).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the number and density of probes spots on the array wherein the number and density of probes is selected based on target and assay for which the array will be used as taught by Pinkel et al. (Column 4, lines 6-33) to the array of Letsinger et al. for the obvious benefits of providing a target and assay specific array to thereby optimize assay conditions and maximize experimental results. It is noted that *In re Aller*, 220 F.2d 454,456, 105 USPQ 233,235 states where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation.

8. Claims 53, 59 and 77 are rejected under 35 U.S.C. 103(a) as being unpatentable over Letsinger et al. (U.S. Patent No. 5,681,943, issued 28 October 1997) in view of Stratagene (Catalog, 1988, page 39).

Regarding Claim 53, Letsinger et al. teach an array comprising at least on pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides (Column 7, line 65-Column 8, line 21) and they teach the components of the kit and reagent for use in a hybridization assay (Column 7, lines 13-35) but they do not teach the components and reagents combined into a

kit format. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39). It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Letsinger into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

Regarding Claim 59, Letsinger et al. teach the array and hybridization further comprising reagents for generating a labeled target nucleic acid sample (Column 8, lines 5-20) but they do not teach the reagents combined into a kit format. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39). It would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Letsinger into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

Regarding Claim 77, Letsinger et al. teach an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that cooperatively hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides (Column 7, line 65-Column 8, line 21) and they teach the components of the kit and reagent for use in a hybridization assay (Column 7, lines 13-35) but they do not teach the components and reagents combined into a kit format. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39). It would have been obvious to one

having ordinary skill in the art at the time the invention was made to combine the method of Letsinger into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

9. Claims 11 and 70 are rejected under 35 U.S.C. 103(a) as being unpatentable over Letsinger et al. (U.S. Patent No. 5,681,943, issued 28 October 1997) in view of Lockhart et al. (U.S. Patent No. 6,040,138, filed 15 September 1995).

Regarding Claim 11, Letsinger et al. teach an array comprising at least on pattern of probe oligonucleotide spots stably associated with the surface of a solid support, wherein each probe spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides (Column 7, line 65-Column 8, line 21) but they do not teach the array further comprises at least one mismatch probe.

Regarding Claim 70, Letsinger et al. teach an array comprising at least one pattern of probe oligonucleotide spots stably associated with the surface of a solid support wherein each probe oligonucleotide spot consists of a mixture of a plurality of 2 or more unique oligonucleotides of different sequence that cooperatively hybridize to the same target nucleic acid to produce a complex made up of said target nucleic acid and 2 or more unique oligonucleotides (Column 7, line 65-Column 8, line 21) but they do not teach the array further comprises at least one mismatch probe. However, Lockhart et al. teach a similar array comprising a pattern of unique oligonucleotide probes attached to a surface of a solid support wherein the probes are attached to the support in a matrix of positionally defined regions

(Column 2, lines 60-65) and wherein the microarray comprises at least one mismatch probe wherein the mismatch probes provide a control against which hybridization signal may be compared (Column 3, lines 30-38). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the arrays of Letsinger et al. to include mismatch control probes as taught by Lockhart et al. wherein hybridization signal intensity is compared to mismatch hybridization for the expected benefit of facilitating signal analysis by comparing the signal to the mismatch control probe to thereby improve and facilitate hybridization analysis as taught by Lockhart et al. (Column 3, lines 30-38).

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
July 25, 2001